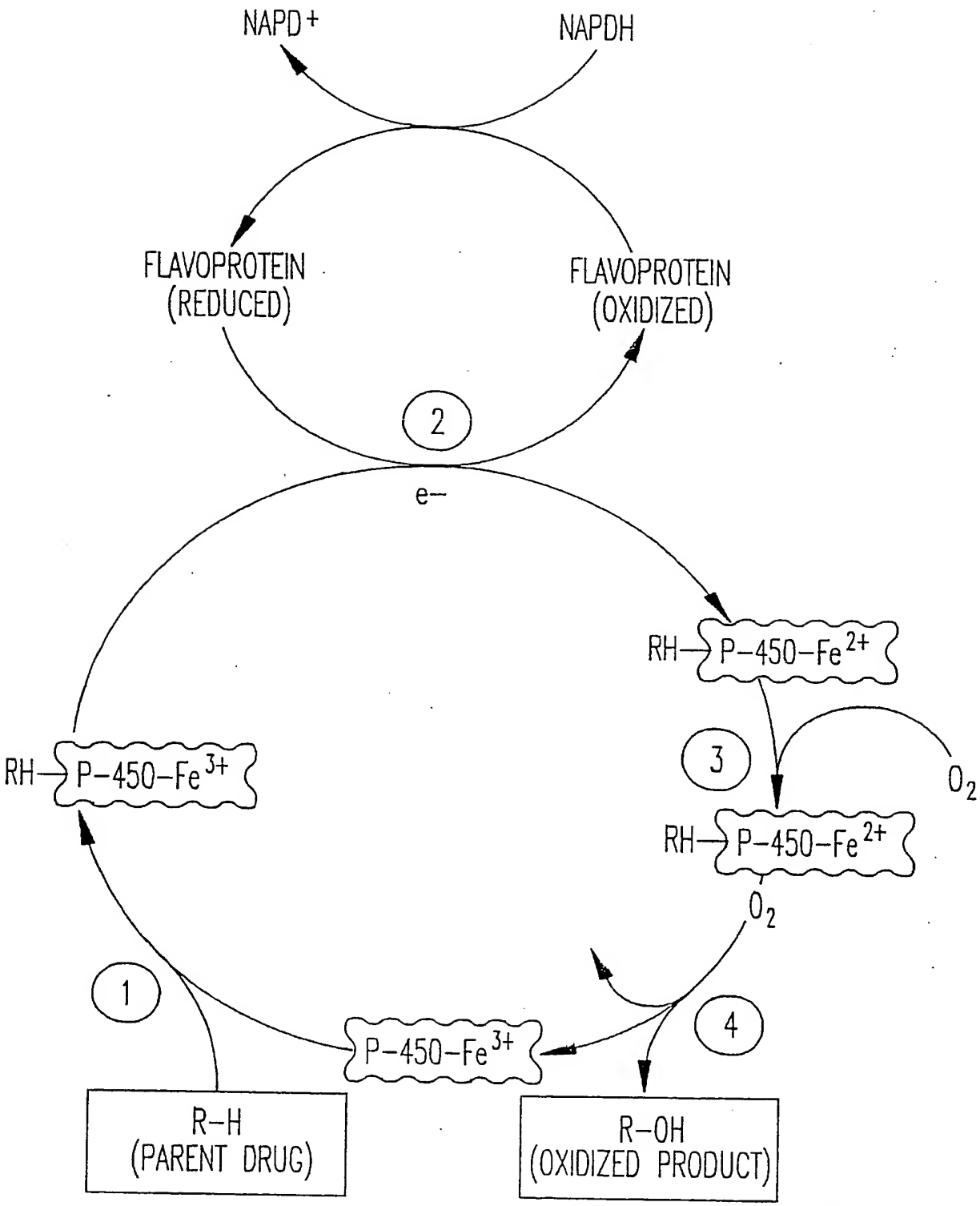
NAPD+
NAPDH
FLAVOPROTEIN (REDUCED)
FLAVOPROTEIN (OXIDIZED)
2
e–
RH—P-450-Fe2+
3
O2
RH—P-450-Fe3+
RH—P-450-Fe2+
O2
1
4
P-450-Fe3+
R-H (PARENT DRUG)
R-OH (OXIDIZED PRODUCT)

Fig. 1

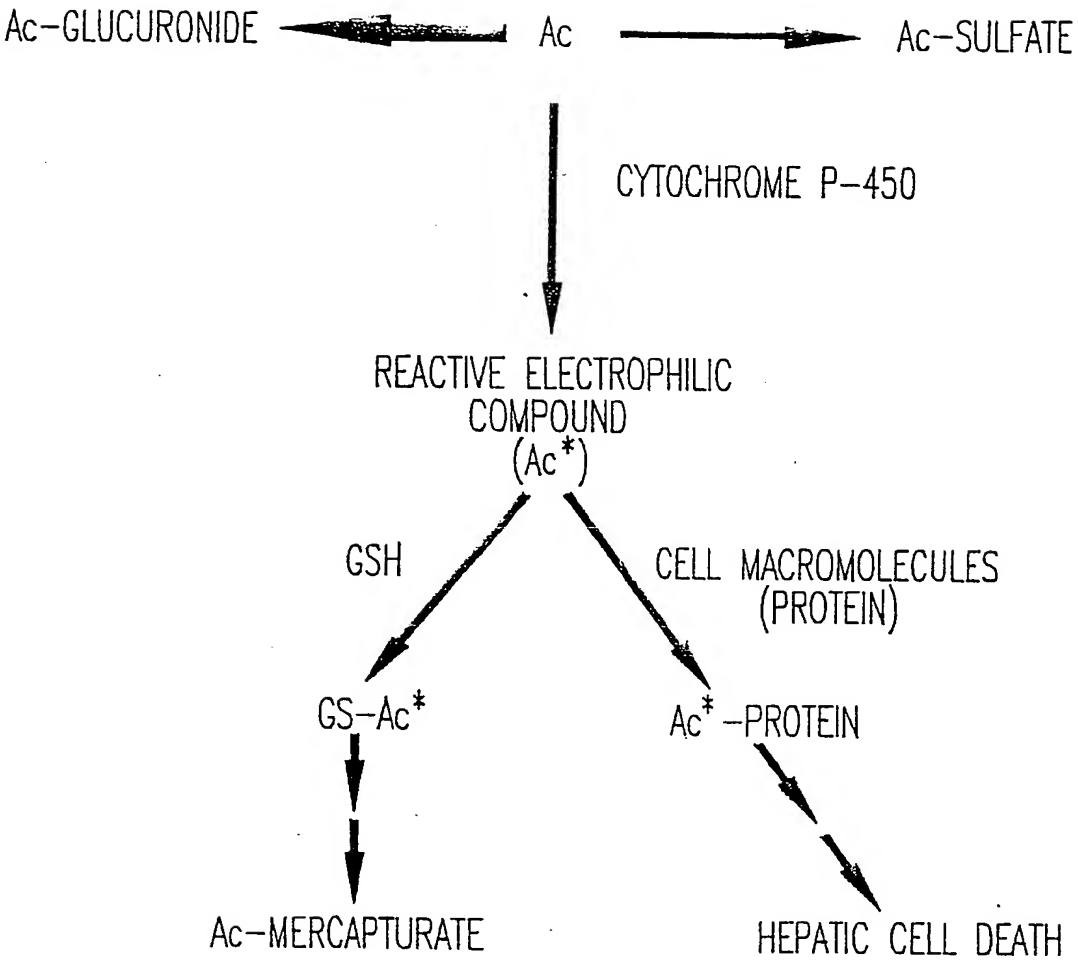
Ac-GLUCURONIDE
Ac
Ac-SULFATE
CYTOCHROME P-450
REACTIVE ELECTROPHILIC COMPOUND (Ac*)
GSH
CELL MACROMOLECULES (PROTEIN)
GS-Ac*
Ac*-PROTEIN
Ac-MERCAPTURATE
HEPATIC CELL DEATH

Fig. 2

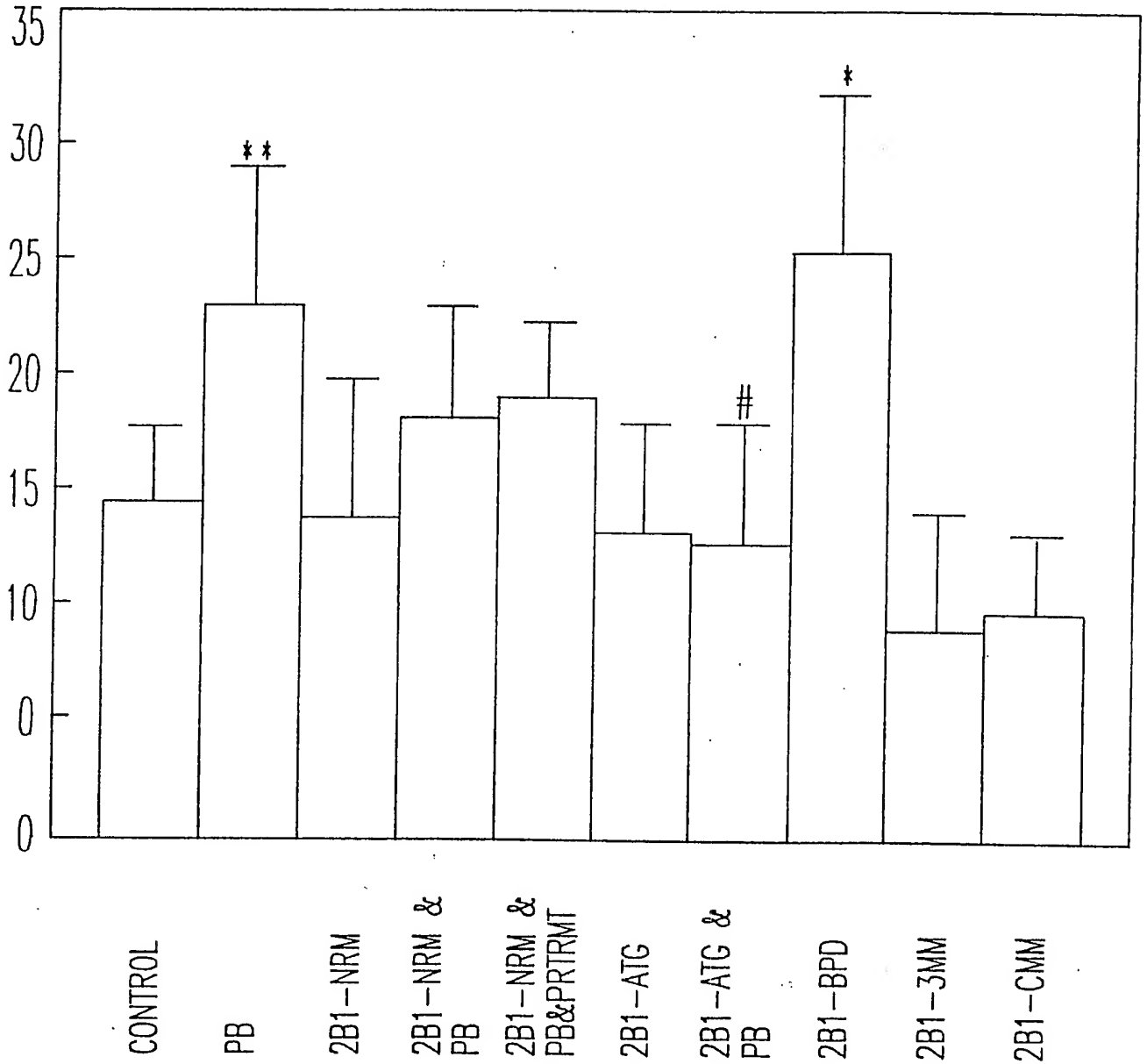
35
30
25
20
15
10
0
0
**
*
#
CONTROL
PB
2B1-NRM
2B1-NRM & PB
2B1-NRM & PB&PRTRMT
2B1-ATG
2B1-ATG & PB
2B1-BPD
2B1-3MM
2B1-CMM

Fig.3

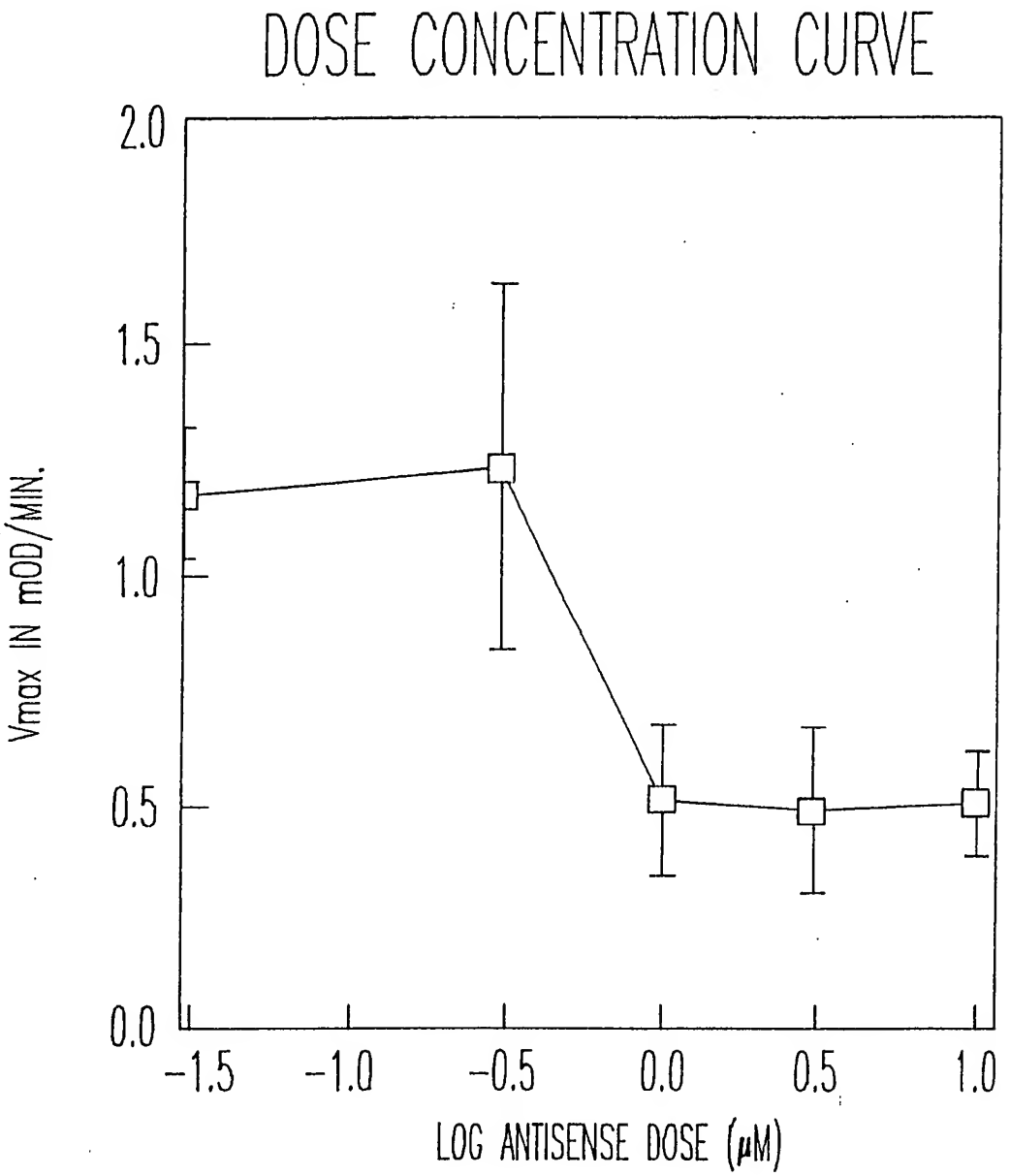
DOSE CONCENTRATION CURVE
2.0
1.5
1.0
0.5
0.0
Vmax IN mOD/MIN.
-1.5
-1.0
-0.5
0.0
0.5
1.0
LOG ANTISENSE DOSE (μM)

Fig. 4

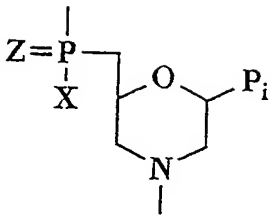

Fig. 5A

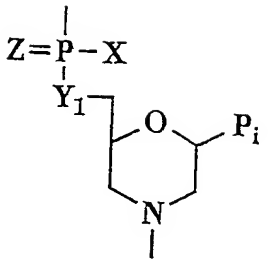

Fig. 5B

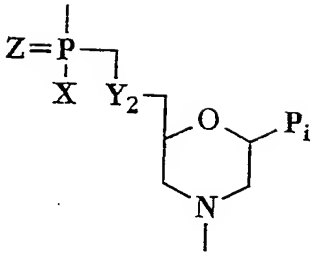

Fig. 5C

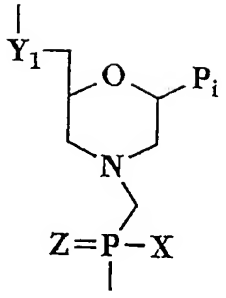

Fig. 5D

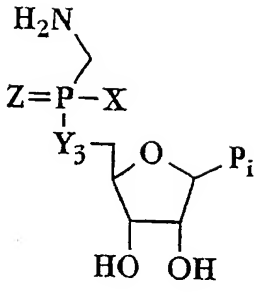

Fig. 5E

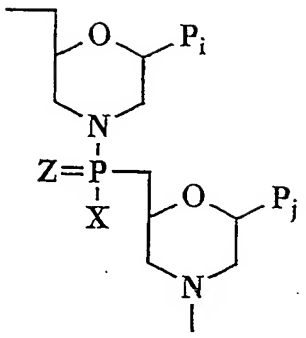

Fig. 6A-A

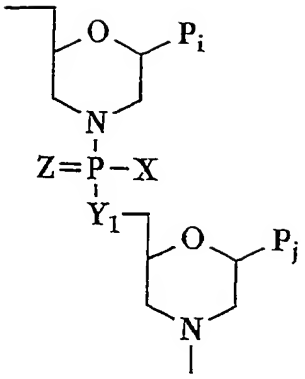

Fig. 6B-B

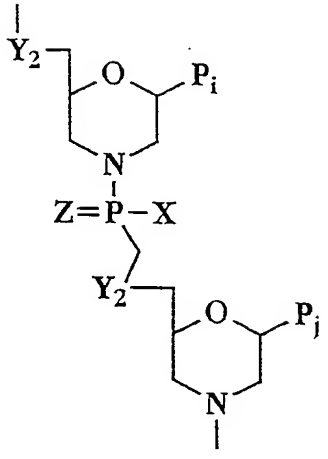

Fig. 6C-C

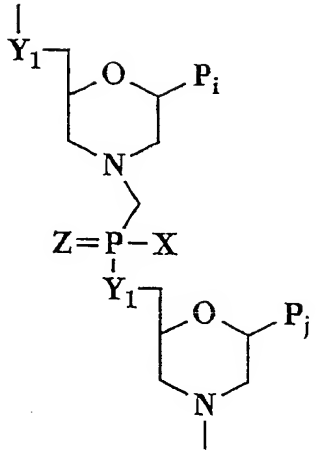

Fig. 6D-D/E-E

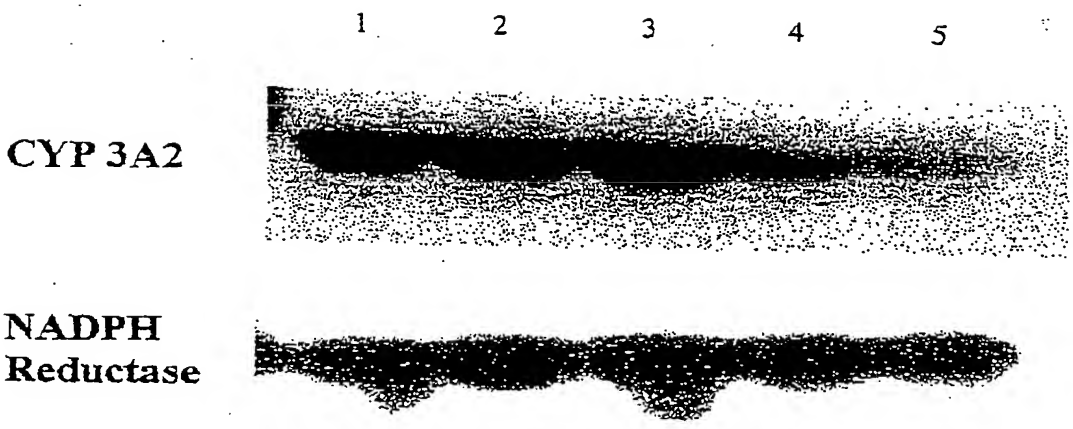

Fig. 7

BEST AVAILABLE COPY